## *REMARKS*

Claims 1, 3, 4 and 6-34 are pending in this application. Claims 1, 4, 6 and 7 have been amended. Claim 2 has been cancelled without prejudice or disclaimer of the subject matter therein. Claims 9-34 have been withdrawn as being a non-elected subject matter.

Claim 1 has been amended to incorporate the limitation of claim 2, now cancelled; claim 4 has been amended to delete "derivatives" from "Cy-dyes derivatives" and to add "DNA GREEN phosphoamidite"; and claims 6 and 7 have been amended to replace "base(s)" with "nucleotide(s)". Support for the amendments can be found throughout the specification and the claims as originally filed including, for example, Example 2.

The amendments to and cancellation of claims are solely for advancing prosecution. Applicants, by amending or cancelling any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert the original claim scope of any claim amended herein, in a continuing application.

No new matter has been introduced to this application within the meaning of 35 U.S.C. §132.

In view of the following, further and favorable consideration is respectfully requested.

***I. Claim interpretation***

Applicants note the Examiner's indication that some claim terms have no definition thereof in the present application. In this regard, Applicants respectfully submit that according to the Examiner's indication, the phase "replace at least a base" in claim 1 has been amended to read "is connected with the middle region of an oligonucleotide instead of a base," and the term "base" in claims 6 and 7 has been amended to "nucleotide."

***II. Rejection of claim 4 under 35 USC §112, first paragraph, written description and enablement requirements***

As basis for maintaining this rejection, the Examiner indicates at page 2 of the Official Action that "[R]egarding the rejection of claim 4 under 35 U.S.C. 112, first paragraph, written description and enablement, Applicants argue that amendments to the claims ... describe a single derivative of a cyanine dye ... However, a single derivative is not representative of thousands of possible species, since the term "cyanine dye" alone encompasses a large number of different dies."

Applicants traverse this rejection. The test under 35 U.S.C. 112, first paragraph, for determining compliance with the written description requirement is whether the application clearly conveys that an applicant has invented the subject matter which is claimed. *In re Barker*, 194 USPQ 470, 473 (CCPA 1977); MPEP 2163. Also, the applicant must convey to the public what the applicant claims as the invention so that the public may ascertain if the patent applicant claims anything in common use or already known. MPEP § 2163. Lastly, the specification must convey

that the applicant was in possession of the invention. MPEP § 2163. The Examiner is respectfully reminded that the Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *In re Wertheim*, 191USPQ 90, 98 (CCPA 1976).

The enablement provision of the Patent Act requires that the patentee provide a written description of the invention "in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same." 35 U.S.C. § 112, first paragraph (2000). The purpose of this requirement is to ensure that "the public knowledge is enriched by the patent specification to a degree at least commensurate with the scope of the claims." *Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1195-96 (Fed. Cir. 1999); *see also* Donald S. Chisum, 3 *Chisum on Patents* § 7.01 (2002).

Applicants submit that claim 4, as currently amended, fully complies with both the written description requirement and the enablement requirement under 35 USC § 112, first paragraph, since amended claim 4 does ***not*** contain the term "derivatives" for the cyanine dye.

Regarding "DNA GREEN phosphoamidite" as presented in claim 4, Applicants submit that ***Example 2***, titled ***"Synthesis of DNA Green Phosphoramidite"*** describes the preparation of a phosphoramidite containing fluorescent material as

shown by chemical formula 1 therein. Example 2 further describes that the phosphoramidite containing fluoresecent material is represented as DNA GREEN phosphoramidite. See page 20 and 21 of the PCT publication of the present application.

Accordingly, the present specification as originally filed describes the subject matter of claim 4 where the florescent dye is DNA GREEN phosphoamidite in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same support. Also, from the description of Example 2, it is clear that the present Applicants was in possession of the subject matter of claim 4 where the florescent dye is DNA GREEN phosphoamidite at the time of invention.

As such, currently pending claim 4 complies with the written description requirement as well as the enablement requirement under 35 USC §112, first paragraph. Reconsideration and withdrawal of these rejections are therefore respectfully requested.

### *III. Rejection of claims 1-4, 6 and 7 under 35 USC §102(b) as being anticipated by Mergny et al. as evidenced by Morgan et al.*

As basis for maintaining this rejection, the Examiner indicates at page 3 of the Official Action that "[A]pplicants argue that *Mergny et al.* do not teach the newly added limitation of claim 1, wherein the fluorescent dye "replaces at least a base of a nucleotide. Applicants did not define what it means for a dye "to replace a base."

Does it mean that there is a gap in the phosphodiester backbone and the dye is attached there, or that a base of a nucleotide is replaced by a dye? In view of the above, since Mergny et al. teach attaching dyes to both 3' and 5' ends of an oligonucleotide, they inherently teach replacing a base with the dye." Further, the Examiner indicates at page 6 of the Official Action that it is evidenced by Morgan et al. that fluorescence of ethidium bromide increases when it is bound to double-stranded DNA.

Applicants respectfully traverse this rejection. The test for anticipation is whether each and every element as set forth is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP §2131. The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP §2131. The elements must also be arranged as required by the claim. *In re Bond*, 15 USPQ2d 1566 (Fed. Cir. 1990).

In the present application, claim 1 recites "A fluorescent probe for real-time detection of amplification of nucleic acid, wherein a fluorescent dye of which intensity of fluorescence is varied when the dye is intercalated into a double-stranded nucleic acid, is ***connected with the middle region of an oligonucleotide instead of at least a base of the oligonucleotide*** of which base sequence is complementary with at least a part of said nucleic acid." [Emphasis added] Claims 3, 4, 6 and 7 are

directly dependent from claim 1, and thus contain all the limitations of claim 1.

*Mergny et al.* describes oligonucleotides covalently linked to a fluorescent dye. The fluorescent dye in the probe of *Mergny et al.,* however, is connected to oligonucleotide, and in this regard the fluorescent dye should be ***connected either at 3' or at 5' end of the oligonucleotide*** for a Fluorescence Energy Transfer. In contrast, in the present claims, the fluorescent dye is connected in the ***middle region*** of the oligonucleotide; and the dye is connected with the oligonucleotide instead of at least a base of the oligonucleotide, not between nucleotides.

In addition, it should be noted that $T_m$ (melting temperature) of a probe is determined by the number of bases. $T_m$ decreases by 2-3 °C as one base is deleted. $T_m$ decreases more when an internal base is deleted than when a 3'- or 5'-end base is deleted. If the length of the probe is same, the base number of the presently claimed probe is ***less*** than that of *Mergny et al.* by the above structural difference, and $T_m$ of the presently claimed probe is ***lower*** than that of *Mergny et al.* Thus, the presently claimed probe is intercalated into the ds DNS or RNA easily.

Accordingly, *Mergny et al.* teach a fluorescent probe having a different structure from the claimed prove.

*Morgan et al.,* which is cited by the Examiner as evidencing that the fluorescence of ethidium bromide increases when it is bound to double stranded DNA, do not remedy the deficiencies of *Mergny et al.* Nowhere does the Morgan et al. reference describe the connection of fluorescent dyes to a base of oligonucleotide in

the middle region of the oligonucleotide.

Accordingly, Applicants submit that *Mergny et al.* do not anticipate claims 1, 3, 4, 6 and 7 as presently pending in the present application. Reconsideration and withdrawal of these rejections is therefore respectfully requested.

***CONCLUSION***

In view of the foregoing, Applicants submit that the pending claims are in condition for allowance. Early notice to this effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed such contact will expedite the prosecution of the application.

If the Examiner has any questions or comments regarding this matter, he is welcomed to contact the undersigned attorney at the below-listed number and address.

In the event this paper is not timely filed, applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

**THE NATH LAW GROUP**

Date: February 23, 2010

Tanya E. Harkins
Reg. No. 52,993
Mih Suhn Koh
Reg. No. 65,085
Customer No. 20529

**THE NATH LAW GROUP**
112 S. West Street
Alexandria, Virginia 22314
Tel: (703) 548-6284
Fax: (703) 683-8396